



导读:本期高伟坚博士将向读者介绍“西登哈姆氏舞蹈病(小舞蹈病)”和“相关的神经精神障碍大鼠动物模型”。此文献向读者解读了:一篇高质量的文章,作者的原始构思和巧妙实验方法。有助于读者清楚地认识到由想法到实验设计的完成和论文撰写工作。

Topics of interest – ‘Developing novel animal models for complex disorders’ Edition 2

While it can be challenging for any research team to develop a novel, reproducible animal model for their investigations into complex disorders or syndromes, it goes without mentioning that simple, clear and well designed experiments based on fundamental hypotheses remain key to achieving a high level of success. In this article, I bring your attention to some excellent research carried out by Brimberg et al (2012), whose work helped produce a novel rat model for the study of neuropsychiatric disorders, specifically Sydenham’s chorea (SC) and Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections (PANDAS).

Brimberg et al (2012) elegantly designed a series of experiments based on the ‘molecular mimicry’ hypothesis. In relation to SC and PANDAS, antibodies produced by the host system following a Group A β -hemolytic Streptococci (GABH) infection, are found to, not only target the dominant group A streptococcal epitope N-acetyl-beta-D-glucosamine (GlcNAc), but also cross react with extracellular antigens on neuronal cells (such as lysogangliosides) after crossing the blood brain barrier. These series of events are thought to underlie the pathogenesis of the disease state causing the primary symptoms, such as involuntary movements and neuropsychiatric disturbances.

Importantly, the novel rat model of SC produced by Brimberg et al (2012) closely resembled the human condition and was validated through a series of experimental measures, which included (i) behavioural – *rats demonstrated loss of fine motor control and compulsive behaviours which are similar to clinical the signs* (ii) pharmacological – *the drugs used to treat symptoms in patients were administered to GABH infected rats and were found to alleviate the induced stereotypical behaviours* (iii) molecular – *antibody deposition was found present in specific regions of the rat brain, measurements of neurotransmitter levels showed changes in dopamine and glutamate consistent with the data in patients, and, sera from the rat model and patients were both found to cause activation of the same second messenger signalling cascades*. An important aspect of this high quality paper is that the authors went on to utilise their novel animal model to further understand the pathophysiology of SC and PANDAS. They did this through demonstrating that dopamine receptor subtypes D1 and D2 were also targets of the antibodies produced by the host system following infection.

Based on a clear hypothesis, the execution of simple experiments produced high impact research that remains highly regarded in this field. Importantly, the work exemplifies basic methods of high quality research, which can be followed by all researchers in the different fields of science.

References

Brimberg et al., 2012. Behavioral, pharmacological, and immunological abnormalities after streptococcal exposure: a novel rat model of Sydenham chorea and related neuropsychiatric disorders. *Neuropsychopharmacology*. 37 (9), 2076 – 87.

栏目主持:李秦